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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/434,708	11/05/99	BAND	H B0801/7159(E

HM22/0102

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EXAMINER	
EWOLDT,G	
ART UNIT	**PAPER NUMBER**
1644	12

DATE MAILED: 01/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/434,708	Waban et al.
Examiner	**Group Art Unit**
Gerald Ewoldt	1644

☒ Responsive to communication(s) filed on *Nov 27, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-7, 9, 11, and 50* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7, 9, 11, and 50* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6, 9*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election of Group I, claims 1-7, 9, 11, and 50, in Paper No. 11, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-7, 9, 11, and 50 are being acted upon.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-7, 9, 11, and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant asserts the nucleic acids of SEQ ID NOS:1 and 3 "make it possible for the artisan to diagnose a disorder characterized by an aberrant [including mutant] expression of cbl-SL," and further asserts the nucleic acids of the instant claims can be used in a "method for treating subjects expressing a mutant cbl-SL." Applicant further asserts that aberrant cbl-SL expression is associated with essentially every known cancer (see page 28, lines 11-24). However, the specification discloses no evidence (i.e., working examples) of *any* association between aberrant expression of cbl-SL and *any* cancer. Thus said diagnosis or treatment would be highly unpredictable and require undue experimentation.

The specification further fails to provide sufficient evidence to establish that *any* CBL-SL protein is even actually expressed. Example 3 establishes only that an antibody generated to a synthetic peptide derived from a purported open reading frame itself derived from an EST sequence binds a band of "about 50 kD" in certain cell lines. Note that the specification

discloses only the production of a recombinantly expressed fusion protein; no *in vivo* biological activity is established for the naturally expressed protein (should it exist) or any of the claimed variants or fragments thereof.

Regarding variants and fragments, the recitation in claim 1 of nucleic acids encoding polypeptides comprising "deletions, additions, and substitutions", as well as nucleic acids "which hybridize under stringent conditions to a molecule consisting of a nucleic acid of SEQ ID NO:1," opens the claim to include nucleic acid molecules that encode a virtually unlimited number of polypeptides. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, Mikayama et al. teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human macrophage migration inhibitory factor (MIF) by a single amino acid residue (see Figure 1 in particular). Yet, Mikayama et al. teaches further that GIF is unable to carry out the function of MIF and MIF does not demonstrate GIF bioactivity (see Abstract in particular). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al., teaches that a single Glu to Val substitution in the subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (see pages 126-128, section 6-3A and page 230, paragraph bridging columns in particular). Further, the relationship between the sequence of a protein and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). Thus, the combined references serve to demonstrate that predicting the function of polypeptides comprising "deletions, additions, and substitutions", as well as polypeptides encoded by nucleic acids "which hybridize under stringent conditions" is highly uncertain and would require undue experimentation.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of sufficient working examples, the unpredictability of the

art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

5. Claims 1-7, 9, 11, and 50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of any cbl-SL nucleic acids including those with deletions, substitutions, additions; or fragments, unique fragments or compliments; or cbl-SL nucleic acid molecules consisting of sequences of 2-7, 8, 10, 12, 14, 16, 18, 2,0, 22, 24, 26, 28, 30, 50, 75, 100, or 200 contiguous nucleotides of deletions, substitutions, additions, fragments, unique fragments or compliments of the nucleic acids of SEQ ID NOS:1 or 3; other than SEQ ID NOS:1 or 3. Neither is there sufficient written description to show that Applicant was in possession of a nucleic acid encoding polypeptides consisting of immunogenic fragments of SEQ ID NO:1, other than a nucleic acid encoding the peptide of SEQ ID NO:10. The instant claims encompass a virtually unlimited number of nucleic acids while the specification discloses just 2. The specification fails to even disclose whether or not most of the claimed embodiments actually exist. One of skill in the art would therefore conclude that the specification fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-7, 9, 11, and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, "a nucleic acid molecule which hybridizes under stringent conditions to a molecule consisting of a nucleic acid of SEQ ID NO:1" is indefinite because the hybridization conditions have not been defined. The specification discloses hybridization conditions on page 11 "for example". Said conditions are not limiting, thus the claim is indefinite.

8. No claim is allowed.

9. References C16-C18 have been lined through and have not been considered because copies of the sequences have not been included.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
December 29, 2000

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600